

REMARKS/ARGUMENTS:

Claim Amendments

Claims 1-12, 14 and 16-18 are currently pending.

Claim 12 is currently amended. Support for the amendment of claim 12 can be found at least at page 3, line 26 - page 4, line 14 of the original specification. No new matter, nor new issues, are raised by the amendment.

Claim 14 has been amended to correct grammatical errors.

Claim Rejections under 35 U.S.C. § 112, second paragraph

1. The Examiner rejected claims 12, 14 and 16-18 under 35 USC § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. More specifically, the Examiner asserted that it was not clear how an amino acid sequence "contains" amino acid residues. The Examiner suggested amending the claim to recite "amino acid sequence comprising SEQ ID NO: 2.

According to MPEP § 2111.03, "[t]he transitional term 'comprising'... is synonymous with 'including,' 'containing,' or 'characterized by,' [and] is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ('like the term 'comprising,' the terms 'containing' and 'mixture' are open-ended.').

Despite the above, in the interest of expediency Applicant has amended claim 12 to recite "amino acid sequence comprising SEQ ID NO:2" as suggested. Withdrawal of the rejection is, thus, courteously requested.

2. The Examiner also rejected Claims 12, 14 and 16-18 under 35 USC § 112, second paragraph, as allegedly being indefinite. More specifically, the Examiner asserted that the phrase "an amino acid sequence of SEQ ID NO: 2," as recited in claim 12 rendered it indefinite because "it was not clear whether the claimed polypeptide comprised a fragment of SEQ ID NO: 2 or the

full length of the amino acid sequence of SEQ ID NO: 2. The Examiner then suggested amending the claim to replace “an” with “the.” Applicant respectfully traverses the rejection.

Contrary to the Examiner’s assertion, it is claim 14, and not claim 12, that recites the language noted by the Examiner. Accordingly, Applicant has amended claim 14 to recite “...at least one of the following amino acid substitution patterns in ~~an amino acid sequence of~~ SEQ ID NO: 2.”

Withdrawal of the rejection is, thus, courteously requested.

3. The Examiner rejected Claims 12 and 16-18 under 35 USC § 112, second paragraph, on grounds that the phrase “isolating resulting hydroxylated product from the medium,” of claim 12 was unclear. More specifically, the Examiner asserted that, “[m]odified P450 monooxygenases hydroxylate both at the terminal and subterminal positions of a carboxylic acid [such that] a) it [was] not clear to the Examiner how Applicants distinguish or direct the enzyme to make only subterminally hydroxylated products and b) it is not clear to the examiner the steps of isolating subterminally hydroxylated carboxylic acids from terminally hydroxylated carboxylic acids. Applicant respectfully traverse the rejection.

Claim 12 is not limited to “making only subterminally hydroxylated aliphatic carboxylic acids,” but rather recites a process for the production of subterminally hydroxylated aliphatic carboxylic acids, which process can include the co-production of terminally hydroxylated carboxylic acids. Accordingly, claim 12 is not incomplete as it does not purport to be concerned with isolating subterminally hydroxylated carboxylic acids from terminally hydroxylated carboxylic acids. Accordingly, Applicant has amended claim 12 to recite “isolating the resulting hydroxylated products from the medium” to emphasize/clarify that the process is not only concerned with isolating subterminally hydroxylated carboxylic acids from terminally hydroxylated carboxylic acids.

In view of the above, withdrawal of the rejection is courteously requested.

4. The Examiner rejected Claim 12, 14 and 16-18 under 35 USC § 112, second paragraph, as being indefinite and grounds that the phrase "is derived from *Bacillus megaterium*" was unclear. More specifically, the Examiner asserted that it was unclear whether the monooxygenase "derived from *Bacillus megaterium* encompassed a single specific enzyme (SEQ ID NO: 2)" or "whether it encompasses recombinants, variants and mutants of SEQ ID NO: 2 or modified monooxygenase from any other source and labeled as monooxygenase derived from *Bacillus megaterium*." Applicant respectfully traverses the rejection.

Applicant respectfully submits that the phrase "is derived from *Bacillus megaterium*" is not intended to refer to that fact that the sequence is limited to being physically isolated from *B. megaterium*, but rather, as described in the paragraph bridging pages 2 and 3 of the specification, is intended to refer to the fact that the sequence is preferably based on the sequence of *B. megaterium*, and can contain functionally equivalent mutations, variants, etc.

Withdrawal of the rejection is, thus, courteously requested.

5. The Examiner also rejected Claim 14 under 35 USC § 112, second paragraph, on grounds that it was not clear if the amino acid substitutions in groups "F87A L188K A74G and R47F," were in the alternative or all-inclusive. Applicant has amended Claim 14 to provide proper punctuation.

Withdrawal of the rejection is courteously requested.

Claim Rejections under 35 U.S.C. § 112, first paragraph

1. The Examiner rejected Claims 12, 14 and 16-18 under 35 USC § 112, first paragraph, on grounds that the specification "fails to describe a representative species of the genus comprising variants and mutants of any recombinants, variants and mutants of any cytochrome P450 monooxygenase derived from SEQ ID NO: 2 used to produce subterminally hydroxylated aliphatic carboxylic acids....Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 12, 14 and 16-18."

Applicant has amended claim 12 to further recite “a nucleic acid sequence encoding a monooxygenase which is derived from *Bacillus megaterium* cytochrome P450 monooxygenase BM-3 with an amino acid sequence comprising SEQ ID NO:2 containing one functional mutation in each of amino acid sequence positions 87 and 188 and, optionally, at least one additional functional mutation in one of amino acid sequence positions 26, 47, 72, 74 and 354, wherein: Phe 87 is replaced by at Val, Ala or Leu; Leu 188 is replaced by Asn, Gln, Arg, Lys, Ala, Gly, Ser or Trp; Ala 74 is replaced by Val or Gly; Arg 47 is replaced by His, Tyr or Phe; Val 26 is replaced by Ser or Thr; Ser 72 is replaced by Ala, Leu, Ile or Gly; or, Met 354 is replaced by Ser or Thr...”

Reconsideration of the rejection is respectfully requested in view thereof.

2. The Examiner also rejected Claims 12, 14 and 16-18 under 35 USC § 112, first paragraph, as not enabling a method “for the production of subterminally hydroxylated aliphatic carboxylic acids wherein said method encompasses the use of any cytochrome P450 monooxygenase derived from SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims...it would require undue experimentation.”

As noted above, Applicant has amended claim 12 to further recite “a nucleic acid sequence encoding a monooxygenase which is derived from *Bacillus megaterium* cytochrome P450 monooxygenase BM-3 with an amino acid sequence comprising SEQ ID NO:2 containing one functional mutation in each of amino acid sequence positions 87 and 188 and, optionally, at least one additional functional mutation in one of amino acid sequence positions 26, 47, 72, 74 and 354, wherein: Phe 87 is replaced by at Val, Ala or Leu; Leu 188 is replaced by Asn, Gln, Arg, Lys, Ala, Gly, Ser or Trp; Ala 74 is replaced by Val or Gly; Arg 47 is replaced by His, Tyr or Phe; Val 26 is replaced by Ser or Thr; Ser 72 is replaced by Ala, Leu, Ile or Gly; or, Met 354 is replaced by Ser or Thr...”

Reconsideration of the rejection is respectfully requested in view thereof.

Claim Rejections under 35 U.S.C. § 102

The Examiner rejected Claims 12, 14, and 16-18 under 35 USC § 102(b) as being anticipated by Graham-Lorence et al. More specifically, the Examiner asserts that absent objective evidence to the contrary, “because the phrase ‘a derivative of C₈-C₁₂-carboxylic acid’ is...not clear and since the specification does not exclude a 20 carbon fatty acid...arachidonic acid has been interpreted as a derivative of a C₈-C₁₂-carboxylic acid.” Applicant respectfully traverses the rejection.

Claim 12 specifically recites “at least one hydroxylatable C₈-C₁₂-carboxylic acid or a derivative thereof, said derivative selected from an alkyl ester, an amide or an anhydride thereof.” (Emphasis added). Accordingly, claim 12 is sufficiently clear on its face with regard to the scope of the claimed derivative. Accordingly, the Examiner’s interpretation that arachidonic acid comprises a derivative of Claim 12 is not reasonable in view of the specification and the explicit recitation of the claims. Accordingly, because Graham Lorence et al. do not disclose “said derivative selected from an alkyl ester, an amide or an anhydride thereof” Graham Lorence do not anticipate Claim 12.

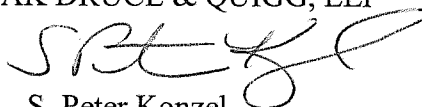
The rejection should be withdrawn.

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Inventor: HAUER et al.
Reply to Office Action of July 27, 2006
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Conclusion

Applicants respectfully submit that the present application is in condition for allowance, which action is courteously requested. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,
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